REMARKS

Applicants gratefully acknowledge the withdrawal of the obviousness rejection under 35 U.S.C. 103(a) based on CA 2,474,902 ("Elbe et al") taken alone or in combination with JP 08/176112 ("Kanji et al") and the obviousness-type double patenting rejection based on copending application Serial No. 10/502,994.

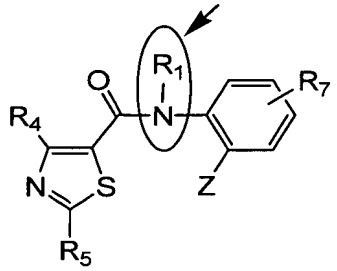
Allowable Subject Matter

Applicants gratefully acknowledge the indication in the Final Office Action that Claims 26, 28, and 29 stand only objected to as being dependent upon a rejected base claim but would be allowable if rewritten in proper independent form. Applicants note for the convenience of the Examiner that Claim 26 is directed to embodiments of Claim 18 in which R^6 represents $-COR^7$ in which R^7 is limited to 4-(difluoromethyl)-2-methyl-1,3-thiazol-2-yl; Claim 28 is directed to embodiments of Claim 18 in which R^6 represents -CHO; and Claim 29 is directed to embodiments of Claim 18 in which R^6 represents specific alkyl or substituted alkyl groups, cycloalkyl groups, or sulfanyl, sulfinyl, or sulfonyl groups but not carbonyl-containing groups within the meaning of $-COR^7$. Applicants maintain that all pending claims, including the base claim, are allowable as written and thus have not amended Claims 26, 28, and 29 as kindly suggested by the Examiner.

Rejection under 35 U.S.C. 103

Claims 18-25, 27, and 29-33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/059086 ("Walter et al"), taken alone or in combination with Kanji et al. Applicants again respectfully traverse.

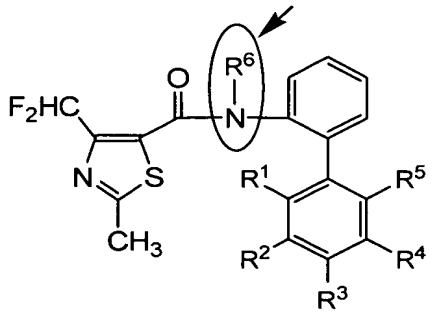
As fully discussed in Applicants' previous Amendments, **Walter et al** discloses certain microbicidal carboxamides, among the many types of which are compounds that can be represented by the formula



(which Applicants again point out is not shown as such in the reference but is pieced together from the general disclosure where A is group (A3) and Q is group (Q1)) in which $\mathbf{R_1}$ (designated by an oval and arrow) can be one of three specific unsaturated

hydrocarbon groups having at least one carbon-carbon multiple bond or COR_3; $\mathbf{R_2}$ is hydrogen or any of several carbon-containing substituents; $\mathbf{R_3}$ is optionally substituted alkyl (in which the substituent can be halogen, alkoxy, or haloalkoxy) or is alkylthio, haloalkylthio, alkoxy, haloalkoxy, alkenyloxy, haloalkenyloxy, alkynyloxy, or haloalkynyloxy; $\mathbf{R_4}$ is optionally fluorinated methyl (including, among other groups, CF_2H) or is chlorine or bromine; $\mathbf{R_5}$ is methyl, CF_3, CH_2OCH_3, or CH_2OCF_3; and **Z** is phenyl or halophenyl, optionally substituted C_5-C_7 cycloalkyl, or a branched alkyl group. See pages 1-2. Walter et al thus encompasses compounds in which A is group (A3), Q is group (Q1), and the bridging amide group can bear a carbonyl group connected to a narrowly defined set of optionally substituted alkyl, alkoxy, alkylthio, alkenyloxy, or alkynyloxy groups (i.e., COR_3).

Applicants, on the other hand, claim thiazolylbiphenylamides of formula (I)



(I)

in which the bridging amide nitrogen atom (again shown by an oval and arrow) is substituted by either (1) non-carbonyl R^6 groups that are entirely different from the unsaturated hydrocarbon groups taught by Walter et al or (2) certain carbonyl-containing R^6 groups.

Applicants assume that the Final Office Action, by indicating that Claim 29 would be allowable if written in independent form, effectively acknowledges that compounds of their invention in which R^6 represents non-carbonyl groups are patentably distinct from Walter et al (and, for that matter, from Walter et al in view of Kanji et al).

Applicants therefore direct attention to embodiments of their invention in which the amide substituent R^6 is a carbonyl-containing $-COR^7$ group. Applicants maintain that such compounds are patentably distinct from those of Walter et al in which A is the thiazolyl group (A3), Q is the phenyl group (Q1), and the bridging amide group is substituted with COR_3. Applicants again note with respect to some of the carbonyl-containing substituents of the claims that the Final Office Action has

affirmed the allowability of narrowly defined carbonyl-substituted compounds within the scope of Claim 26 (in which R^6 represents -COR^7 as long as R^7 is limited to 4-(difluoromethyl)-2-methyl-1,3-thiazol-2-yl) and Claim 28 (in which R^6 represents formyl). Applicants note in this regard that Walter et al also does not disclose compounds in which R_3 is an amino group and thus would not suggest compounds of Applicants' invention in which R^6 is -$CONR^8R^9$. As for other compounds of their invention in which R^6 is -COR^7, Applicants acknowledge that R^6 encompasses carbonyl groups that are in some cases similar to the carbonyl group COR_3 of the reference (for example, where R_3 is (halo)alkyl or (halo)alkoxy) but again respectfully submit that their claimed invention is patentably distinct from Walter et al (even when combined with Kanji et al) when the overall teachings of the reference are viewed in proper context.

It has long been recognized that even structurally similar inventions can be patentably distinct under certain circumstances. E.g., *U.S. v. Adams*, 383 U.S. 39, 148 U.S.P.Q. 479 (1966). For example, a claimed invention is not rendered obvious merely because a reference discloses "compounds having a generic formula which would include [the claimed compounds] if proper selection from among the many possible variables were made as suitable for the claimed purpose." *Ex parte Strobel and Catino*, 160 U.S.P.Q. 352 (P.O. Bd. App. 1968); see also *In re Baird*, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994). This principle is particularly applicable where the properties exhibited by compounds in the relevant art are unpredictable and where, as here, comparative evidence supports a finding of non-obviousness. With respect to the claims now at issue, Walter et al does not describe the particular combination of structural features that characterize the N-carbonyl-substituted embodiments of Applicants' invention nor does the reference show even one example of an N-carbonyl-substituted compound in which A is a thiazole bearing a haloalkyl substituent R_4 other than CF_3. Only by picking and choosing from the host of possible groups disclosed in the reference could one in retrospect arrive at Applicants' specified combination of features. That is, to arrive at Applicants' claimed compounds, it would be necessary to select only thiazoles (A3) from among the five heterocyclic structures of group A and even then only thiazoles in which substituent R_4 is CF_2H; and select only phenyl groups (Q1) from among the six ring structures of group Q and even then only phenyl groups in which substituent Z is phenyl or halophenyl; and select only COR_3 from among the seven possibilities for group R_1

and even then only when R_3 represents certain groups. The reference provides no indication that such selections would provide enhanced properties.

Applicants maintain that this failure of Walter et al to disclose compounds having the specific combination of features that characterize their invention is consistent with the patentability of their invention. Nevertheless, Applicants provided further support for their position by providing comparison data in the first Declaration of Dr. Wachendorff-Neumann showing that their compound of Example 9 – which has both an N-carbonyl group on the amide bridge and a difluoromethyl group in the thiazole moiety – provided significantly enhanced biological activity compared to the comparison compound of Example 4.32 of Walter et al (see page 33) – which has the same N-carbonyl substituent but replaces the trifluoromethyl group in the thiazole moiety with a difluoromethyl group. Applicants thus maintain that their data support the patentability of their claimed invention over the teachings of Walter et al. The Final Office Action, however, states at pages 9-10 that the reference teaches the interchangeability of trifluoromethyl and difluoromethyl groups and again asserts at page 2 and elsewhere that Applicants' Declaration dated February 23, 2007 (i.e., the first Declaration of Dr. Wachendorff-Neumann), is insufficient to overcome the rejection. Applicants again submit that this Declaration does support their position.

First, Applicants respectfully submit that the Final Office Action at pages 3 to 4 again incorrectly interprets the numbering scheme used for the compounds described in the Declaration. In particular, the Final Office Action states that in Table I of the Declaration either the structure shown for "Example 2" is incorrect or the name (i.e., number label) is incorrect and further states that the same numbering error appears in the other tables. Applicants again emphatically point out that the Declaration does not identify "different compounds" in the Declaration. Although Applicants had assumed (see their previous Amendment dated June 12, 2008, at the top of page 10) that the Examiner understood the thorough explanation of this numbering scheme provided in their earlier Amendment dated August 28, 2007, Applicants again provide a detailed explanation for the convenience of the Examiner. The Example numbers used in the Declaration are clearly nothing more than a sequential listing of each test carried out according to the various test protocols, beginning with the first test described in the Declaration (i.e., Example 1 in Table I) and ending with the final test described in the Declaration (i.e., Example 8 in Table IV), all of which example numbers pertain only to the tests described in the

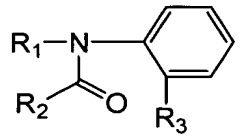
Declaration. Applicants made no representation in the Declaration or in their Amendments that the numbers used in the Declaration were intended to correlate with any of the numbers used in the examples in their specification (or the reference). Quite to the contrary, each Table of the Declaration clearly shows that the odd-numbered examples refer to tests carried out on known compounds described in preparative examples of the cited references. That is, Table I specifically indicates that comparative Example 1 of the Declaration was carried out using Compound 4.32 of WO 2002/059086. [Tables II, III, and IV similarly indicate that Examples 3, 5, and 7, respectively, of the Declaration were carried out using the compound of Example 21 of CA 2474902, the Elbe et al patent no longer at issue.] In short, the odd numbers used in the first Declaration for the comparison examples do not correspond to or even correlate with Examples 1, 3, 5, and 7 of Applicants' specification. Similarly, the even example numbers used in the Declaration do not correspond to or correlate with Examples 2, 4, 6, and 8 of the specification but instead refer to tests carried out on the inventive compound shown in the table. The reason the same structure is displayed for all of the even-number examples in the tables of the Declaration is that the same compound was used in all of these examples. Although not identified in the Declaration by reference to a specific example number from the specification, the compound used for all of the even-number tests is the compound disclosed in Applicants' Ex. 9 (shown in Table 1 at pages 40-41 of the specification). Although the test numbering scheme used in the Declaration may at first seem somewhat confusing, careful reading shows that each table in the Declaration clearly states that the inventive compound is "[a]ccording to the invention" and clearly shows a specific chemical structure that corresponds to the compound identified in Example 9 of the specification. Applicants therefore again submit that the first Declaration of Dr. Wachendorff-Neumann shows what it purports to show as it relates to Walter et al – that an inventive compound having a difluoro-methyl substituent on the thiazole moiety is superior to a known comparison compound that differs only in having a trifluoromethyl substituent.

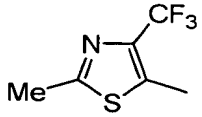
Second, the Final Office Action at page 3 states that Applicants should have provided more data for more compounds. More particularly, the Final Office Action refers to Applicants' Examples 1 and 8 (in which R^6 is acetyl) and Example 9 (in which R^6 is methoxyacetyl) and suggests that Applicants should have compared all of these compounds to Compound 4.20 (in which R_1 is acetyl) and Compounds 4.43

and 4.44 (in which R_1 is methoxycarbonyl) of Walter et al. [Applicants also note that the Final Office Action later refers to Compound 7.03 of the reference, which is not a thiazolyl compound and thus has little if any relevance to the claims at issue.] Aside from the fact that the difference in structure between a methoxyacetyl group and a methoxycarbonyl group means that a comparison between Applicants' compound of Example 9 and Compound 4.43 or 4.44 of Walter et al would have questionable value, Applicants maintain that the direct comparison of their inventive Example 9 with Compound 4.32 of the reference in Table I of Dr. Wachendorff-Neumann's first Declaration is at least as representative and relevant as any other comparison suggested in the Final Office Action. The purpose of the comparison experiment described in Table I was not to show the biological effect of different kinds of amide substituents R^6 – that was the purpose of other experiments presented in this Declaration (i.e., R^6 is methoxyacetyl vs. R^6 is H) and the other Declaration (i.e., R^6 is methyl vs. R^6 is H) – but instead was to show the effect of substitution in the thiazole ring by a difluoromethyl group compared to a trifluoromethyl group. Since Applicants have carried out a directly comparative experiment showing the significance of difluoromethyl substitution in the thiazole moiety, Applicants submit that another test using any other such compound of the reference would be essentially duplicative and unnecessary.

Applicants therefore submit that their claimed invention is patentably distinct from Walter et al taken alone. Applicants also maintain that Kanji et al would not lead those skilled in the art to their claimed invention.

As already fully discussed in Applicants' previous Amendments, **Kanji et al** discloses carboxamides of the formula



in which $\mathbf{R_1}$ can be any of a number of groups, including acyl groups of formulas -CO-R_4 (where R_4 can be alkyl, haloalkyl, or phenoxymethyl) or a second amide moiety -CO-NH-R_5 (where R_5 can be alkyl or phenyl), as well as certain ethers R_6 or alkyl groups R_7; $\mathbf{R_2}$ can be a variety of cyclic groups, including a specific trifluoromethyl-substituted thiazole moiety having the formula 

; and

R_3 can be any of a variety of cyclic or unsaturated groups, including phenyl. The Final Office Action relies on Kanji et al, inter alia, as teaching the interchangeability of the various substituents at the amide nitrogen atom of the disclosed thiazole-containing carboxamides. See Final Office Action at page 6. However, regardless of whether Kanji et al teaches such interchangeability of amide substituents, the reference does not even remotely suggest that the thiazole moiety could bear any haloalkyl substituent other than CF_3, which, as discussed above, Applicants have shown confers inferior properties relative to the CHF_2 group that characterizes their invention. In the absence of any suggestion of a difluoromethyl-substituted thiazolyl moiety, Kanji et al adds nothing that Walter et al does not already disclose that would lead those skilled in the art to their claimed invention.

Applicants therefore respectfully maintain that their invention is not rendered obvious by Walter et al, whether taken alone or in combination with Kanji et al.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

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